UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/044,716	01/11/2002	John Langenfeld	270/070	1276

26259 7590 10/20/2004

LICATLA & TYRRELL P.C.
66 E. MAIN STREET
MARLTON, NJ 08053

EXAMINER	
RAWLINGS, STEPHEN L	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/044,716	LANGENFELD, JOHN	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 June 2002*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-64* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The preliminary amendment filed June 25, 2002 is acknowledged and has been entered.

2. Claims 1-64 are pending in the application and are currently subject to restriction.

Election/Restrictions

3. Restriction to one of the following inventions is required under 35 U.S.C. 121:

Group I. Claims 2 and 5-10, drawn to a method for treatment of cancer comprising administering to a patient a therapeutically effective amount of a polypeptide that binds specifically to bone morphogenetic protein-2 (BMP-2), classified in class 514, subclass 2.

Group II. Claims 3 and 4, drawn to a method for treatment of cancer comprising administering to a patient a therapeutically effective amount of a polypeptide that binds specifically to a receptor of BMP-2, classified in class 514, subclass 2.

Group III. Claim 11, drawn to a method for treatment of cancer comprising administering to a patient a therapeutically effective amount of an antibody that binds BMP-2, classified in class 424, subclass 138.1.

Group IV. Claims 12, 13, and 37-45 drawn to a method for treatment of cancer comprising administering to a patient a therapeutically effective amount of an antisense oligonucleotide or an expression vector encoding an antisense oligonucleotide, wherein said oligonucleotide binds a BMP-2 encoding nucleic acid sequence, classified in class 514, subclass 44.

Group V. Claims 23 and 26-30, drawn to a method for treatment of cancer comprising administering to a patient a therapeutically effective amount of an expression vector encoding an inhibitor of an activity of BMP-2, wherein said inhibitor is a polypeptide that binds BMP-2, classified in class 514, subclass 44.

Group VI. Claims 24 and 25, drawn to a method for treatment of cancer comprising administering to a patient a therapeutically effective amount of an expression vector encoding an inhibitor of an activity of BMP-2, wherein said inhibitor is a polypeptide that binds a receptor of BMP-2, classified in class 514, subclass 44.

Group VII. Claims 46-49 are drawn to an article of manufacture comprising a polypeptide that binds specifically to BMP-2, which cannot be classified, since the chemical and biologic nature of the BMP-2 activity inhibitor has not been specified.

Note: If Applicant were to amend claims 46-49 to link patentably distinct inventions, wherein said BMP-2 activity inhibitor is selected from those inhibitors to which the claims 1, 14-22, and 31-36 are directed, claims 46-49 would be subject to further restriction in accord with the above restriction of claims 1-45.

Group VIII. Claims 50-64, drawn to a method for the diagnosis of cancer in a patient comprising measuring the level of BMP-2 in the patient, classified in class 435, subclass 7.1 or class 424, subclass 9.1+.

4. Claims 1, 14-22, and 31-36 are linking claims.

Claims 1 and 14-19 are linking claims, which are presently considered to link claims drawn a method for treatment of cancer comprising administering a BMP-2 activity inhibitor, wherein said inhibitor is selected from the group consisting of (a) a polypeptide that binds specifically to BMP-2, (b) a polypeptide that binds specifically to a receptor of BMP-2, (c) an antibody to BMP-2, (d) an antisense oligonucleotide that binds at least a portion of a BMP-2 nucleic acid sequence.

Claims 20-22 and 31-36 are a linking claim, which are presently considered to link claims drawn to a method for treatment of cancer comprising administering an expression vector encoding a BMP-2 activity inhibitor, wherein said inhibitor is selected from the group consisting of (a) a polypeptide that binds specifically to BMP-2, (b) a polypeptide that binds specifically to a receptor of BMP-2, (c) an antisense oligonucleotide that binds at least a portion of a BMP-2 nucleic acid sequence.

The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s). Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim depending from or otherwise including all the limitations of the allowable linking claims will be entitled to examination in the instant application. Applicants are advised that if any such claims depending from or including all the limitations of the allowable linking claims are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

5. The inventions are distinct, each from the other because of the following reasons:

The inventions of Groups I-VI and VIII are patentably distinct methods, each from the other.

The inventions of Groups I-VI are patentably distinct inventions, each from the other, because, although each is a method for treating cancer, each is a materially different method, because each comprises administering a distinct product that has a unique structure and functions in a unique manner.

The inventions of Groups I and II are patentably distinct methods comprising administering distinct products, since the invention of Group I comprises administering a polypeptide that binds BMP-2 and inhibits its function, whereas the invention of Group II comprises administering a polypeptide that binds to a receptor of BMP-2 to inhibit the function of BMP-2. The polypeptides that bind either BMP-2 or its receptor are functionally different molecules. Furthermore, a polypeptide that binds to BMP-2 to inhibit its activity will not also bind a receptor of BMP-2; and a polypeptide that binds a receptor of BMP-2 to inhibit the activity of BMP-2 will not also bind BMP-2. Therefore, it follows that the polypeptides that bind either BMP-2 or its receptor are also structurally distinct molecules. Accordingly, the inventions of Groups I and II are patentably distinct inventions.

The search necessary to examine the invention of Group I is not the same, nor is it coextensive with the search needed to examine the invention of Group II, and vice verse, since, for example, a different set of key words would be used to as a query in searching the databases of relevant technical literature. In addition, although inventions in both groups comprise administering inhibitors of BMP-2 activity, their modes of operation are different and divergent and, because of their different and divergent modes of operation, they have acquired a different status in the art. Accordingly, it would be unduly burdensome to have to search both the inventions of Groups I and II.

Since the inventions of Groups I and II are patentably distinct and since having to search both inventions would constitute a serious burden, it is proper to restrict the inventions. See MPEP § 803.

Similarly, the inventions of Groups II and III are patentably distinct inventions, since the invention of Group II comprises administering a polypeptide and the invention of Group III comprises administering an antibody. Although the inhibitors of both of the inventions are types of "polypeptides", an antibody generally comprises four

polypeptides: two light chains and two heavy chains that interact to form an antigen-binding domain capable of recognizing and binding to an antigen. The administered polypeptide of Group I (e.g., noggin) is a polypeptide of a single chain. The inventions of Groups II and III thus comprise administering structurally distinct molecules; furthermore, the inventions comprise administering functionally distinct molecules, since the administered polypeptides of Group II bind a receptor of BMP-2 and the administered antibodies of Group III bind BMP-2. Accordingly, the inventions of Groups II and III are patentably distinct inventions.

In addition, the inventions of Groups II and III have acquired a separate status in the art, as evidenced by their different classifications. Consequently, the search necessary to examine the invention of Group II is not the same, nor is it coextensive with the search needed to examine the invention of Group III, and vice versa.

Since the inventions of Groups II and III are patentably distinct and since having to search both inventions would constitute a serious burden, it is proper to restrict the inventions. See MPEP § 803.

The inventions of Groups I and III are patentably distinct inventions, because the invention of Group I comprises administering a polypeptide, whereas the invention of Group III comprises administering an antibody. Although both the inventions comprise administering a type of polypeptide that binds BMP-2 to inhibit its activity, the inventions comprise administering structurally distinct products and consequently there is no correlation between any structural feature of the products and their common functional feature. The antibodies of Group III generally comprise four polypeptides: two light chains and two heavy chains that interact to form an antigen-binding domain capable of recognizing and binding to an antigen. The polypeptides of Group I are polypeptides of a single chain, which form a structural and functional domain that interacts with BMP-2 by a mechanism distinct from the mechanism by which an antibody binds an antigen.

The inventions of Groups I and III have acquired a separate status in the art, as evidenced by their different classifications. Consequently, the search necessary to examine the invention of Group I is not the same, nor is it coextensive with the search needed to examine the invention of Group III, and vice versa.

Since the inventions of Groups I and III are patentably distinct and since having to search both inventions would constitute a serious burden, it is proper to restrict the inventions. See MPEP § 803.

The inventions of any one of Groups IV-VI and any of the inventions of Groups I-III are patentably distinct from the other, because the inventions of Groups IV-VI comprise administering polynucleotides, whereas the inventions of Groups I-III comprise administering polypeptides or antibodies. Polypeptides or antibodies and polynucleotides are chemically distinct products, since polypeptides or antibodies are composed of polymers of amino acids, whereas polynucleotides are composed of polymers of nucleotides. Any relationship between a polynucleotide and a polypeptide is dependent upon the information provided by the nucleotide sequence of the polynucleotide, as it corresponds to an "open reading frame" encoding the amino acid sequence of the polypeptide. However, the administered polynucleotides of Group IV do not encode any of the administered polypeptides or antibodies of the Groups I-III; the administered polynucleotides of Group V do not encode any of the administered polypeptides or antibodies of Groups II or III, respectively; and the administered polynucleotides of Group VI do not encode any of the administered polypeptides or antibodies of Groups I or III, respectively.

Furthermore, a polypeptide can be produced by means, other than the recombinant means by which a polynucleotide encoding a polypeptide might be used to produce the polypeptide, since a polypeptide can be produced (or isolated) by biochemical means, including, for example, affinity chromatography. In addition, while the polynucleotide might encode the polypeptide, generally, it can also encode another polypeptide using the information provided by an alternative open reading frame; and furthermore, since a polynucleotide can be used as a probe in hybridization-based analyses, the information provided by a polynucleotide can be used isolate different polynucleotides encoding polypeptides, which have amino acid sequences that differ from the amino acid sequence encoded by the disclosed polynucleotide. Consequently, the disclosed relationship between a polynucleotide capable of encoding a polypeptide and the polypeptide is not exclusive, since either the claimed polynucleotide or the

claimed polypeptide can also be related to other polynucleotides or polypeptides, which are materially and chemically different from the claimed inventions. Therefore, any of the inventions of Groups IV-VI and any of Groups I-III comprise administering distinct products.

The inventions of Groups IV-VI and any of the inventions of Groups I-III have acquired a separate status in the art, as evidenced by their different classifications, and the search performed in examining claims drawn to a polynucleotide is a different from the search performed in examining claims drawn to a polypeptide. Apart from the searching patent databases using the patent classification of the claimed subject matter, a thorough search of the technical literature is particularly pertinent, and since such a search is performed by a series of key word queries of relevant databases, each search would be performed using a different set or series of key words. Therefore, the search and considerations necessary in examining the merit of claims of any of Groups I-III would not suffice to provide adequate information regarding the merit of the claims of any of Groups IV-VI, and vice versa, since the searches are not the same, nor are they one coextensive in scope and nature. Because different searches would have to be performed to examine the inventions of each of the groups, an examination of more than one would constitute a serious burden.

Since the inventions of any of Groups I-III and any of the inventions of Groups IV-VI are patentably distinct from the other and because the examination of any two or more of the inventions could not be made without serious burden, it is proper to restrict each from the other. See MPEP § 803.

In summary, the inventions of Groups I-VI are patentably distinct inventions, each from the other, because each is a materially different method comprising administering a distinct product that has a unique structure and functions in a unique manner. The structural and functional differences between these products have been described above. Briefly, each different product has a unique structure; and none of the products share a structural feature that is disclosed as essential to the function of the product (i.e., to its ability to inhibit an activity of BMP-2). As each different product administered in practicing the different inventions has a different structure, function, and/or mode of

action, each method has achieved a different status in the art, as evidenced in some instances by their different classifications or in other instances, by their art-recognized divergent structures, functions, and/or modes of operation. Because of the different products used and their different modes of action, the search required to consider any one of the inventions of Groups I-VI is not the same, nor is it coextensive with the search necessary to consider any of the others. Moreover, because there appears no correlation between any particular feature of the varied structures of the different products and their common function, a search and consideration of the generic invention, or of more than one of the inventions would be unduly burdensome.

Any one of the inventions of Groups I-VI and the inventions of Group VIII are patentably distinct inventions. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects. See MPEP §§ 806.04 and 808.01. The instant specification does not disclose that any one of the inventions of Groups I-VI and the inventions of Group VIII are useable together. The claimed methods for the treatment of cancer (the invention of Group I-VI) and the claimed method for the diagnosis of cancer (the invention of Group VIII) are unrelated because they are materially different, as each utilizes different products, and comprise distinct process steps; accordingly, each method has a different mode of operation. The purpose or objective of the inventions is different, since the intended purpose of the inventions of Groups I-VI is to treat cancer, whereas the intended purpose of the inventions of Group VIII is to diagnose cancer.

Searching any of the invention of Group I-VI and the invention of Group VIII would be unduly burdensome, because the inventions have acquired a separate status in the arts, as evidenced by their separate classifications and their art-recognized divergence in objectives and modes of operation. Moreover, because the necessary searches are not the same, nor are they coextensive in nature and scope with one another, having to search any one of the inventions of Groups I-VI together with the inventions of Group VIII would constitute a serious burden.

Since the inventions of any of Groups I-VI and the inventions of Group VIII are patentably distinct, each from the other, and because the examination of more than one of the inventions could not be made without serious burden, it is proper to restrict each from the other. See MPEP § 803.

Inventions in group VII and any of inventions I-IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the product as claimed, namely the article of manufacture comprising a bone morphogenetic protein-2 activity inhibitor (e.g., polypeptide, antibody, an antisense oligonucleotide, and expression vector encoding a polypeptide) can be used in a materially different process of using that product, such as the process of producing an antibody that binds specifically to the inhibitor using the polypeptide as an immunogen, the process of detecting a nucleic acid molecule in a sample by Northern blot analysis using the antisense oligonucleotide as a probe, the process of purifying the polypeptide to which the antibody binds by affinity chromatography, or the process of producing the polypeptide encoded by the expression vector by transfecting a host cell with the expression vector.

The inventions of Group VII and the inventions of Groups V-VI and VIII are unrelated because the products of Group VII are not specifically used or otherwise involved in the processes of Groups V-VI and VIII.

6. Because these inventions are distinct for the reasons given above and also because the search required for any one group is not required for any other group and/or the inventions have acquired a separate status in the art as shown by their different classification or their recognized divergent subject matter, searching more than

one invention encompassed by the claim would constitute a serious burden; therefore, restriction for examination purposes as indicated is proper.

7. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

8. This application contains claims directed to the following patentably distinct species of the claimed invention:

The inventions of Groups I and V comprise patentably distinct species of invention, wherein the polypeptide that binds to BMP-2 is selected from the group of polypeptides, or a fragment thereof, consisting of (a) human Noggin (SEQ ID NO: 4), (b) mouse Noggin (SEQ ID NO: 6), (c) Chordin, (d) Cerberus 1 homolog, and (e) Gremlin.

To the extent that the claims of any of Groups I and V are drawn to any one of the polypeptides, the claims are drawn to patentably distinct species of invention, because each of the polypeptide is a distinct polypeptide having a unique amino acid sequence. Although each polypeptide is disclosed as capable of inhibiting the activity of BMP-2, there is no disclosed correlation between any one substantial structural feature that may be shared by the different polypeptides, which is essential to this particular common function, and the function. Because each polypeptide is structurally distinct from the others, the search necessary to examine claims drawn to any one of the polypeptides is therefore not the same as or coextensive with the search needed to examiner the claims drawn to any other of the polypeptides. Consequently, the need to search claims drawn to more than one polypeptide, and thus the need to search more than one species of invention, would be unduly burdensome. It is proper to restrict species of inventions, where the species of invention are patentably distinct and the examination of more than one could not be made without serious burden.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Applicant must do so by specifically identifying the polypeptide (i.e., the polypeptide of (a), (b), (c), (d), or (e), as recited above) to which the claims of the elected invention will be drawn during prosecution on the merits.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

9. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Conclusion

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642

slr
October 13, 2004